Complete Summary

GUIDELINE TITLE

National Academy of Clinical Biochemistry laboratory medicine practice guidelines: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes.

BIBLIOGRAPHIC SOURCE(S)

Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB, Wu AH, Christenson RH, Apple FS, Francis G, Tang W, National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. Clin Chem 2007 Apr;53(4):552-74. [198 references] PubMed

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GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Acute coronary syndrome (ACS)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine
Pathology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS)

TARGET POPULATION

Patients with suspected or known acute coronary syndrome (ACS)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient history
2. Physical examination
3. Electrocardiogram
4. Risk stratification
5. Measurement of cardiac biomarkers
    - Cardiac troponin
    - Creatinine kinase MB
    - Myoglobin
    - High sensitivity C-reactive protein
    - Brain type natriuretic peptide (BNP)
    - N-terminal pro-BNP

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic tests
- Mortality rate
- Incidence of myocardial infarction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These National Academy of Clinical Biochemistry (NACB) guidelines were developed rigorously; however it was possible to include only papers published in the English language. The specified method for developing the evidence base for recommendations listed involved use of PubMed, EMBASE, and other databases that were not necessarily published. Systematic methods were used whenever available; searches were first set to be sensitive to avoid missing papers of possible interest, and then narrowed to sort through the literature in order to enhance specificity. The writing group contacted recognized experts to assure that important evidence had not been missed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

C - Expert Consensus was the primary basis for the recommendation

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Academy of Clinical Biochemistry's (NACB) Laboratory Medicine Practice Guidelines (LMPG) for use of cardiac markers in coronary artery diseases were published in July of 1999. Since production of this initial document, numerous published studies and presented data have added significantly to the knowledge base for cardiac biomarkers. This increased knowledge has substantially expanded the scope of recommendations for cardiac biomarker utilization since the 1999 document, and in particular has required the inclusion of recommendations regarding biomarkers that extend beyond myocardial necrosis. Toward addressing these advances and their impact on biomarker utilization in clinical practice, the NACB appointed a chair and members of a LMPG committee that was charged with the overall objective of revising and extending the earlier recommendations by establishing modern guidelines for Utilization of Biomarkers in Acute Coronary Syndrome and Heart Failure. This LMPG is aimed at providing analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS), heart failure and point-of-care measurement and logistics of providing ACS biomarker data for patient

care; guidance for interpretation of biomarkers in etiologies other than ACS and Heart Failure is included as well.

These guidelines and their recommendations are structured into six chapters that include Chapter 1: Clinical Utilization of Biomarkers in Acute Coronary Syndromes (ACS); Chapter 2: Analytical Issues of ACS Biomarkers; Chapter 3: Clinical Utilization of Biomarkers of Heart Failure; Chapter 4: Analytical Issues of Heart Failure Biomarkers; Chapter 5: Point of Care Testing and Logistics; and Chapter 6: Cardiac Biomarkers and Other Etiologies. Each chapter was spearheaded by a writing group, which was a subset of the overall committee. In addition, other ad hoc expertise contributed to the writing group of some subsections and chapters to optimize the content and quality of the guidelines. The "questions" for each chapter are in the form of issues addressed and specified in the organization of each individual chapter. The chapter design of the guidelines was used to facilitate finding guidance by users; this format was also used, in part, to provide an easy and focused procedure for updating the guidelines in the future. Also, the chapter design allowed publication of sections in appropriate laboratory medicine and clinical specialty journals.

Stakeholder involvement in development and refinement of these guidelines was substantial. The guideline team was comprised of laboratory medicine, ACS cardiology experts, and heart failure cardiology experts. As these guidelines target acutely ill patients, Emergency Medicine stakeholders were represented by a specialist; it is also noteworthy that all of the laboratory professionals and cardiology experts on the guideline committee have substantial interaction, knowledge, and publications in the area of laboratory and clinical medicine in the Emergency Medicine environment.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Modified American College of Cardiology/American Heart Association Classifications: Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or treatment.

> **Class IIa**: Weight of evidence/opinion is in favor of usefulness/efficacy.
>
> **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Stakeholder involvement in development and refinement of these guidelines was substantial. To further enhance stakeholder input, draft revisions of the Guidelines were prepared and placed for comment on the National Academy of Clinical Biochemistry (NACB) World Wide Web site (http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/DraftGuidelines/BioHearFailure/). The draft Laboratory Medicine Practice Guidelines (LMPG) and suggested revisions were also presented for public and stakeholder comment at the October 2004 Arnold O. Beckman Conference titled *Cardiac Markers: Establishing Guidelines and Improving Results*. Refer to Table 1 of the Preamble to the original guideline document for a list of the various stakeholder groups that agreed to examine the documents and were represented at the conference.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the weight of evidence (A-C) and the summary of indications (Classes I, II, IIa, IIb, III) are presented at the end of the "Major Recommendations" field.

Note from the National Academy of Clinical Biochemistry (NACB) and the National Guideline Clearinghouse (NGC)*: The Laboratory Medicine Practice Guidelines (LMPG) for utilization of biochemical markers in acute coronary syndromes and heart failure* have been divided into individual summaries. In addition to the current summary, the following are available:

- Chapter 2: Analytical issues for biochemical markers of acute coronary syndromes
- Chapter 3: Clinical utilization of cardiac biomarker testing in heart failure
- Chapter 4: Analytical issues for biomarkers of heart failure
- Chapter 5: Point of care testing, oversight and administration of cardiac biomarkers for acute coronary syndromes
- Chapter 6: Use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure

Use of Biochemical Markers in the Initial Evaluation of Acute Coronary Syndrome (ACS)

Diagnosis of Myocardial Infarction

Recommendations for use of biochemical markers for diagnosis of myocardial infarction (MI)

Class I

1. Biomarkers of myocardial necrosis should be measured in all patients who present with symptoms consistent with ACS. **(Level of Evidence: C)**
2. The patient's clinical presentation (history, physical exam) and electrocardiogram (ECG) should be used in conjunction with biomarkers in the diagnostic evaluation of suspected MI. **(Level of Evidence: C)**
3. Cardiac troponin is the preferred marker for the diagnosis of MI. Creatine kinase MB (CK-MB) by mass assay is an acceptable alternative when cardiac troponin is not available. **(Level of Evidence: A)**
4. Blood should be obtained for testing at hospital presentation followed by serial sampling with timing of sampling based on the clinical circumstances. For most patients, blood should be obtained for testing at hospital presentation and at 6 to 9 h. **(Level of Evidence: C)**
5. In the presence of a clinical history suggestive of ACS, the following are considered indicative of myocardial necrosis consistent with MI: **(Level of Evidence: C)**
    a. Maximal concentration of cardiac troponin exceeding the 99th percentile of values (with optimal precision defined by total coefficient of variation [CV] <10%) for a reference control group on at least 1 occasion during the first 24 h after the clinical event (observation of a rise and/or fall in values is useful in discriminating the timing of injury).
    b. Maximal concentration of CK-MB exceeding the 99th percentile of values for a sex-specific reference control group on 2 successive samples (values for CK-MB should rise and/or fall).

Class IIB

1. For patients who present within 6 h of the onset of symptoms, an early marker of myocardial necrosis may be considered in addition to a cardiac troponin. Myoglobin is the most extensively studied marker for this purpose. **(Level of Evidence: B)**
2. A rapid "rule-in" protocol with frequent early sampling of markers of myocardial necrosis maybe appropriate if tied to therapeutic strategies. **(Level of Evidence: C)**

Class III

1. Total creatine kinase (CK), CK-MB activity, aspartate amino transferase (AST, [serum glutamic oxaloacetic transaminase] SGOT), beta-hydroxybutyric dehydrogenase, and/or lactate dehydrogenase should not be used as biomarkers for the diagnosis of MI. **(Level of Evidence: C)**
2. For patients with diagnostic ECG abnormalities on presentation (e.g., new ST-segment elevation), diagnosis and treatment should not be delayed while awaiting biomarker results. **(Level of Evidence: C)**

Early Risk Stratification
Recommendations for Use of Biochemical Markers for Risk Stratification in ACS

Class I

1. Patients with suspected ACS should undergo early risk stratification based on an integrated assessment of symptoms, physical exam findings, ECG findings, and biomarkers. **(Level of Evidence: C)**
2. A cardiac troponin is the preferred marker for risk stratification and, if available, should be measured in all patients with suspected ACS. In patients with a clinical syndrome consistent with ACS, a maximal (peak) concentration exceeding the 99th percentile of values for a reference control group should be considered indicative of increased risk of death and recurrent ischemic events **(Level of Evidence: A)**.
3. Blood should be obtained for testing on hospital presentation followed by serial sampling with timing of sampling based on the clinical circumstances. For most patients, blood should be obtained for testing at hospital presentation and at 6 to 9 h. **(Level of Evidence: B)**

Class IIA

1. Measurement of high-sensitivity C-reactive protein (hs-CRP) may be useful, in addition to a cardiac troponin, for risk assessment in patients with a clinical syndrome consistent with ACS. The benefits of therapy based on this strategy remain uncertain. **(Level of Evidence: A)**
2. Measurement of brain-type (B-type) natriuretic peptide (BNP) or N-terminal pro-BNP (NTproBNP) may be useful, in addition to a cardiac troponin, for risk assessment in patients with a clinical syndrome consistent with ACS. The benefits of therapy based on this strategy remain uncertain. **(Level of Evidence: A)**

Class IIB

1. Measurement of markers of myocardial ischemia, in addition to cardiac troponin and ECG, may aid in excluding ACS in patients with a low clinical probability of myocardial ischemia. **(Level of Evidence: C)**
2. A multimarker strategy that includes measurement of 2 or more pathobiologically diverse biomarkers in addition to a cardiac troponin may aid in enhancing risk stratification in patients with a clinical syndrome consistent with ACS. BNP and hs-CRP are the biomarkers best studied using this approach. The benefits of therapy based on this strategy remain uncertain. **(Level of Evidence: C)**
3. Early repeat sampling of cardiac troponin (e.g., 2 to 4 h after presentation) may be appropriate if tied to therapeutic strategies. **(Level of Evidence: C)**

Class III

Biomarkers of necrosis should not be used for routine screening of patients with low clinical probability of ACS. **(Level of Evidence: C)**

Use of Biochemical Markers in the Management of Non-ST Elevation ACS (NSTEACS)

Clinical Decision-making

Recommendations for the use of biochemical cardiac markers for therapeutic decision-making.

Class I

Among patients with a clinical history consistent with ACS, an increased concentration of cardiac troponin should prompt application of ACS management guidelines for patients with indicators of high risk. **(Level of Evidence: B)**

Class III

1. Application of management guidelines for ACS should not be based solely on measurement of natriuretic peptides. **(Level of Evidence: C)**
2. Application of management guidelines for ACS should not be based solely on measurement of CRP. **(Level of Evidence: C)**

Use of Biochemical Markers in the Management of ST-Elevation MI (STEMI)

Biochemical Marker Measurement after the Diagnosis of Acute MI
Recommendations for Measurement of Biochemical Markers of Cardiac Injury after the Diagnosis of MI

Class I

1. Once the diagnosis of acute MI is ascertained, testing of biochemical markers of injury at a reduced frequency (e.g., every [Q]6 to 10 h x 3) is valuable to qualitatively estimate the size of the infarction and to facilitate the detection of complications such as reinfarction. **(Level of Evidence: C)**

Class IIA

2. CK-MB is the preferred marker for detection of reinfarction early after the index event when the concentration of cardiac troponin is still increased. **(Level of Evidence: C)**

Class IIB

3. Cardiac troponin may be used as an alternative to CK-MB for detection of reinfarction early after the index event. Serial measurement of troponin is usually necessary to facilitate the discrimination of a new increase in concentration. **(Level of Evidence C)**

Definitions:

Weight of Evidence

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Summary of Indications

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate utilization of biochemical markers in the diagnosis, risk stratification, and management of acute coronary syndromes (ACS)

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The materials in this publication represent the opinions of the authors and committee members, and do not represent the official position of the National Academy of Clinical Biochemistry (NACB). The National Academy of Clinical Biochemistry is the academy of the American Association for Clinical Chemistry.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB, Wu AH, Christenson RH, Apple FS, Francis G, Tang W, National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. Clin Chem 2007 Apr;53(4):552-74. [198 references] PubMed

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jul (revised 2007 Apr)

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

National Academy of Clinical Biochemistry Writing Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

National Academy of Clinical Biochemistry (NACB) Writing Group Members: David A. Morrow, Christopher P. Cannon, Robert L. Jesse, L. Kristin Newby, Jan Ravkilde, Alan B. Storrow, Alan H.B. Wu, and Robert H. Christenson

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Ad Hoc members of the committee for selected sections: Allan S. Jaffe, Mayo Clinic, Rochester, Minnesota, USA; Alan S. Maisel, University of California at San Diego, San Diego, California, USA; Mauro Panteghini, University of Milan, Milan, Italy

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Other than modest funding from the National Academy of Clinical Biochemistry/American Association for Clinical Chemistry (NACB/AACC), development of these guidelines was a volunteer activity. Thus the guidelines are editorially independent from any funding body.

All potential conflicts of interest for the NACB guidelines committee and ad hoc members of the writing committees are listed at the following: http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/PublishedGuidelines/ACSHeart/heartpdf.htm.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Preamble. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for utilization of biochemical markers in acute coronary syndromes and heart failure. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2007. p. 1-3.

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 11, 2008. The information was verified by the guideline developer on April 2, 2008.

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